



Newborn Screening Quality Assurance Program

PROFICIENCY TESTING

Cystic Fibrosis Quarterly Report

Volume 4, No. 3

August 2005

INTRODUCTION

The Cystic Fibrosis (CF) proficiency testing (PT) report is the quarterly summary of all data reported within the specified data-reporting period for Quarter 3, 2005. The attached tables provide the certification profiles (Immunoreactive Trypsinogen and DNA) for the distributed specimens, the verification of your reported data, the statistical analysis of the quantitative data, and the frequency distributions summary for presumptive clinical (qualitative) assessments. We distribute this PT report to all participants, state laboratory directors, and program colleagues by request.

On July 11, 2005, a panel of five unknown dried-blood-spot (DBS) specimens enriched with predetermined concentrations of IRT was distributed to 11 laboratories in the United States and 48 laboratories in other countries.

PARTICIPANTS' RESULTS

We processed data from 46 participants. Laboratories were asked to report IRT results in ng/mL blood. For the statistical summary analysis, we did not include data that were outside the 99% confidence interval. There were nine outliers for this survey. Results of our evaluation suggest that the endogenous level of IRT was less than 15 ng/mL blood.

Fifteen laboratories reported using Delfia to measure IRT, 21 used AutoDelfia, 2 used MP Biomedicals (ICN), 3 used BioRad Quantase, 2 used Bioclone, and the remaining 3 reported using "other." The expected IRT values are based on CDC assayed values. IRT is stable in the dried blood matrix. Table 1 illustrates comparability of the recovery of IRT from each specimen by method.

Presumptive clinical classifications (qualitative assessments) may differ by participant because of specific assessment practices. For participants that have provided us with their IRT cutoff value, we applied that cutoff in our final appraisal of the error judgment. Overall, participants reported no false-positive clinical assessments and one false-negative clinical assessment. Domestic and foreign laboratories reported various cutoffs for IRT. The median and mode cutoffs for domestic participants were 92.8 ng/mL blood and 90 ng/mL blood, respectively. The median and mode cutoffs for foreign participants were 74.2 ng/mL blood and 70 ng/mL blood, respectively.

We distributed DBS specimens containing DNA from Epstein-Barr virus-transformed lymphoblastoid cell lines homozygous for $\Delta F508$ in a sheep whole blood matrix (specimen 3585). These specimens were enriched with IRT to create proficiency testing materials that expressed both phenotype (elevated IRT) and genotype ($\Delta F508$) for CF.

Participants were asked to confirm specimens that screened IRT positive. Fifteen laboratories reported DNA confirmatory results. Five laboratories reported using PCR amplification of DNA, 2 used Roche Linear Array, 1 used Innogenetics Auto-LiPA method, 3 used Innogenetics Inno-LiPA method, 1 used Tm Biosciences Tag-It Cystic Fibrosis kit, 2 used Oligonucleotide Ligation Assays, and 1 used the Elucigene ARMS assay. There was one misclassification of CF confirmed clinical assessments. Two laboratories could not report data for specimen 3585 because of problems with amplification. We are continuing to evaluate our methods for preparing these specimens to avoid amplification failures by participants. ♦

The Newborn Screening Quality Assurance Program will ship next quarter's Cystic Fibrosis PT specimens on October 3, 2005. ♦

CDC/APHL

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This program is cosponsored by the Centers for Disease Control and Prevention (CDC)
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NEWBORN SCREENING QUALITY ASSURANCE PROGRAM

CYSTIC FIBROSIS - IRT

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LAB XXX

SPECIMEN CERTIFICATION - IRT

CDC ASSAYED LEVELS

Analyte	Specimen 3581	Specimen 3582	Specimen 3583	Specimen 3584	Specimen 3585
Immunoreactive Trypsinogen CDC Mean Assayed Value (ng/mL blood)	35.5 ± 3.3	10.9 ± 2.8	23.5 ± 1.9	83.5 ± 5.1	149.5 ± 16.4

EXPECTED PRESUMPTIVE CLINICAL ASSESSMENTS

Disorder	Specimen 3581	Specimen 3582	Specimen 3583	Specimen 3584	Specimen 3585
Cystic Fibrosis	1	1	1	NE	2

01 = within normal limits

02 = outside normal limits

NE = clinical assessment not evaluated

DATA VERIFICATION

Analyte	Specimen 3581		Specimen 3582		Specimen 3583		Specimen 3584		Specimen 3585	
Immunoreactive Trypsinogen (ng/mL blood)	Result	Code	Result	Code	Result	Code	Result	Code	Result	Code

01 = within normal limits

02 = outside normal limits

NE = clinical assessment not evaluated

Reviewer's Comments

EVALUATION:

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CYSTIC FIBROSIS - IRT

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OVERALL STATISTICS - IRT

Specimen	N*	Outliers	Mean	UL (95%)	LL (95%)
3581	45	1	37.7	53.8	21.6
3582	44	2	10.6	15.2	6
3583	44	2	21.4	29.6	13.3
3584	43	3	75.4	106.1	44.8
3585	45	1	148.3	212.5	84.1

* Outliers are not included in N.

UL = upper limit

LL = lower limit

FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

Specimen	Within Normal Limits	Outside Normal Limits
3581	46	0
3582	46	0
3583	46	0
3584	17	29
3585	1	45

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CYSTIC FIBROSIS - DNA

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SPECIMEN CERTIFICATION - DNA

CDC IDENTIFIED GENOTYPES

Analyte	Specimen 3581	Specimen 3582	Specimen 3583	Specimen 3584	Specimen 3585
DNA	Wild Type (Normal)	Wild Type (Normal)	Wild Type (Normal)	Wild Type (Normal)	$\Delta F508/\Delta F508$

EXPECTED DNA CONFIRMED CLINICAL ASSESSMENTS

Disorder	Specimen 3581	Specimen 3582	Specimen 3583	Specimen 3584	Specimen 3585
Cystic Fibrosis	1, 4	1, 4	1, 4	1, 4	2

1 = wild type (normal)

2 = cystic fibrosis positive

3 = cystic fibrosis carrier

4 = not tested

DATA VERIFICATION

Analyte	Specimen 3581		Specimen 3582		Specimen 3583		Specimen 3584		Specimen 3585	
	Result	Code	Result	Code	Result	Code	Result	Code	Result	Code
DNA										

1 = wild type (normal)

2 = cystic fibrosis positive

3 = cystic fibrosis carrier

4 = not tested

Reviewer's Comments

EVALUATION:

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CYSTIC FIBROSIS - DNA

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SUMMARY OF PARTICIPANTS' GENOTYPES

Specimen	Genotype	N
3581	Wild Type/Wild Type	2
3582	Wild Type/Wild Type	2
3583	Wild Type/Wild Type	2
3584	Wild Type/Wild Type	11
3585	Δ F508/ Δ F508 Δ F508/Wild Type	12 1

FREQUENCY DISTRIBUTION OF PARTICIPANTS' CLINICAL ASSESSMENTS

Specimen	Wild Type (Normal)	Cystic Fibrosis Positive	Cystic Fibrosis Carrier	Not Tested
3581	2	0	0	13
3582	2	0	0	13
3583	2	0	0	13
3584	11	0	0	4
3585	0	12	1	0

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CYSTIC FIBROSIS - IRT

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IMMUNOREACTIVE TRYPSINOGEN BY METHOD

Table 1. Recovery of IRT (ng/mL blood) by method

Specimen No.	Specimen 3581	Specimen 3582	Specimen 3583	Specimen 3584	Specimen 3585
Expected Value	35.5	10.9	23.5	83.5	149.5
Method (N)					
Delfia (15)	38.8 ± 7.3	10.8 ± 3.3	21.3 ± 4.3	76.8 ± 11.7	150.4 ± 19.0
AutoDelfia (21)	40.6 ± 4.1	10.6 ± 2.1	23.0 ± 3.1	79.4 ± 8.0	159.1 ± 16.2
Bio-Rad (3)	21.2 ± 3.2	5.6 ± 2.7	14.4 ± 1.8	45.4 ± 16.5	79.7 ± 35.4
MP (ICN) (2)	42.5 ± 12.0	12.1 ± 4.0	31.6 ± 8.4	119.5 ± 9.2	173.3 ± 9.5
Bioclone (2)	26.8 ± 1.7	7.9 ± 3.0	18.5 ± 2.1	46.5 ± 12.1	80.9 ± 19.7
Other (3)	29.3 ± 12.8	9.3 ± 0.7	17.7 ± 4.0	48.1 ± 32.5	73.6 ± 9.2

N = Number of observations